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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,724	11/20/2001	Avi J. Ashkenazi	P2730P1C67	1123

35489 7590 03/14/2005

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,724	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-127, 129-131 and 135-143* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *124-127 and 129-131* is/are allowed.

6)☒ Claim(s) *119-123 and 135-143* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/23/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibits A & B*.

DETAILED ACTION

1. Claims 1-118, 128 and 132-134 have been canceled.

Claims 119-127, 129-130, 135 and 137 have been amended.

Claims 139-143 have been added.

2. Claims 119-127, 129-131 and 135-143 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

5. The objection to the specification for containing embedded hyperlinks is withdrawn in view of the amendment to the specification.

6. The rejection of claim 137 under 35 U.S.C. 101 as being drawn to non-statutory subject matter is withdrawn in view of the amendment to the claim.

7. The rejections of claims 119-124, 128 and 132-134, parts a-b, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

8. The rejection of claims 119-123 under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors,

at the time the application was filed, had possession of the claimed invention is withdrawn in view of applicant's arguments and amendments to the claims.

9. The rejection of claims 119-123 and 131-138 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in view of the successful completion of the deposit requirements.

10. The rejection of claims 119-123 and 130-131 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in view of the amendments to the claims. It is noted that this rejection was an enablement rejection, not a utility rejection and not based on "homology" as asserted by applicant.

11. The rejection of claims 119-123 and 132-138 under 35 U.S.C. 102(a) as being anticipated by Ruben et al is withdrawn in view of applicant's entitlement to the priority date of U.S. Provisional application no. 60/096,960, i.e., August 18, 1998.

12. The rejection of claims 119-123 and 132-138 under 35 U.S.C. 102(b) as being anticipated Jacobs et al is withdrawn in view of applicant's arguments for entitlement to the priority date of U.S. Provisional application no. 60/096,960, i.e., August 18, and in view of the new grounds of rejection below.

13. The rejection of claims 132-134 under 35 U.S.C. 102(b) as being anticipated by Edwards et al (WO 99/06439, 2/11/1999) is withdrawn in view of the cancellation of these claims.

14. The rejection of claims 119-123 and 132-138 under 35 U.S.C. 102(b) as being anticipated by Edwards et al (WO 99/06439, 2/11/1999) is withdrawn in view of applicant's entitlement to the priority date of U.S. Provisional application no. 60/096,960, i.e., August 18, 1998.

15. The rejection of claims 119-123 and 132-138 under 35 U.S.C. 102(e) as being anticipated by Edwards et al (U.S. Patent 6,312,922 B1, at least 8/10/1998) is withdrawn in view of the amendments to the claims and in view of the New Grounds of Rejection below.

16. The rejection of claims 132-133 under 35 U.S.C. 102(b) as being anticipated by The 1991 Boehinger Mannheim Catalog is withdrawn in view of the cancellation of the claims.

17. The rejection of claims 132-134 under 35 U.S.C. 102(e) as being anticipated by Studier et al is withdrawn in view of the cancellation of the claims.

New Grounds of Rejections

18. Claims 119-123 and 135-138 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Claims 119-123 are directed to nucleic molecules encoding a polypeptide having at least 80% identity with the polypeptide of SEQ ID NO:387, optionally lacking its associated signal peptide and the extracellular domain of SEQ ID NO:387, wherein the polypeptide stimulates cardiac hypertrophy. The specification discloses a nucleic acid molecule comprising SEQ ID NO:386, which encodes a polypeptide comprising SEQ ID NO:387. The claimed polynucleotide is not supported by either a specific and substantial asserted utility or a well-established utility.

Applicant relies on Example 148 at page 523 of the specification, "Stimulation of Heart Neonatal Hypertrophy (Assay 1)". The asserted utility of Example 148, the therapeutic treatment of various cardiac insufficiency disorders is not specific substantial. The specification teaches that (a positive in the assay occurs when the PRO polypeptide treated myocytes are visually larger on the average than the untreated myocytes" (pg 523). Although the specification teaches that PRO1312 is positive in this assay, the specification does not disclose any specific resulting cell numbers, statistical differences, or the number of repetitions for the assay. For example, there is no indication in the specification as to statistically how much larger the PRO polypeptide treated myocytes are as compared to control. Without this knowledge, which could not be gleaned from the instant specification, one of ordinary skill in the art at the time the invention was made would not have been able to use the information obtained from this

assay in a useful manner. One skilled in the art would be unable to repeat the assay with a compound (such as one of the PRO1312 variants as encompassed by the claims) and determine whether the compound scored positive or negative. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Furthermore, PRO1312 may not necessarily stimulate the neonatal heart hypertrophy condition itself but rather, simply bind LIF or ET-1, which are the factors utilized to induce the hypertrophy. The state of the art is also such that a rat cardiac myocyte cell culture is not an art recognized model for heart hypertrophy, but instead is used to explore the regulation of myocardial cell hypertrophy" (Simpson et al., Circ Res 51:787-801, 1982, last sentence in abstract; Ueyama et al., J Mol Cell Cardiol 32: 947-960, 2000).

The specification also does not disclose, what the utility of causing hypertrophy would be; there is no disclosure of which of "various cardiac insufficiency disorders" might be treatable, nor is it recognized that the assay used is predictive of such. The specification discloses nothing specific and substantial about the encoded polypeptides, therefore the encoded polypeptides have no patentable utility.

19. Claims 119-123 and 135-138 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

20. Claims 119-123 and 135-143 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite for reciting, An isolated nucleic acid encoding a polypeptide having at least 80-99% sequence identity to: (c) a nucleic acid sequence...", because a nucleic acid sequence is chemically different from a polypeptide sequence (e.g., see claim 119, preamble and part (c)). Is the encoded polypeptide of part (c) of the claims compared to the encoded polypeptide recited in the preamble of the claims?

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

22. Claims 119-122 and 135-142 are rejected under 35 U.S.C. 102(a) as being anticipated Jacobs et al (WO 98/32853, 7/30/1998, cited on PTO-892 mailed 6/30/2004).

The response filed 12/23/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that applicant is entitled to the priority of USSN 60/096,960, filed August 18, 1998, which the instant application claims priority to

and the Jacobs art only qualifies under 35 U.S.C. 102(a) and not 102(b). Applicant argues that USSN 60/096,960 simply needs to disclose what is disclosed in the cited reference to support the priority claim and cites the Stempel doctrine for support. This is found persuasive with respect to Jacobs et al previously applied under 35 U.S.C. 102(b), however, as Jacobs was published on 7/30/1998, Jacobs still qualifies under 35 U.S.C. 102(a). Applicant also supplies a declaration under 37 C.F.R. 1.131, which states that copies of the sequencing data for the PRO1312 polypeptide sequence and its encoding nucleic acid sequence are attached to the declaration as Exhibit A and applicant argues at page 19 of the response the "Applicants had cloned and sequenced the nucleic acid and polypeptide of SEQ ID NO:386 and 387 respectively, on **May 29, 1998** which is before the prior art date of July 30, 1998 for Jacobs." Therefore, Jacobs is not prior art under 35 U.S.C. 102(a). In response to these arguments, the declaration is insufficient to establish a priority date of May 29, 1998 because the declaration is not signed by all of the inventors of the rejected claims. Further, even if signed by all inventors, the declaration does not provide the documentary evidence (i.e., Exhibit A is missing) sufficient to establish possession of SEQ ID NO:386 and SEQ ID NO:387 on May 29, 1998 and in the absence Exhibit A would be insufficient to obviate this rejection. Therefore, for purposes of this rejection, the filing date of the instant claims is that of USSN 60/096,960, i.e., August 18, 1998. Accordingly, as the publication date of Jacobs is earlier than the effective filing date of the instant application the rejection is maintained for reasons of record in the previous Office Action.

With respect to newly added claims 139-142, Jacobs et al teach a polypeptide (SEQ ID NO:4, pages 65-66) having at least 97% amino acid identity with SEQ ID NO:387. One of ordinary skill in the art would reasonably conclude that Jacobs polypeptide also possesses the same functional properties as those of the polypeptides claimed and, therefore, it appears that Jacobs has produced a polypeptide having the same functional properties as the claimed polypeptides (i.e., induces chondrocyte redifferentiation). Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed polypeptides with the polypeptide of Edwards, the burden of proof is upon the Applicant's to show a distinction between the structural and functional characteristics of the claimed polypeptides and the polypeptide of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

23. Claims 135-142 are rejected under 35 U.S.C. 102(e) as being anticipated by Edwards et al [a] (U.S. Patent 6,312,922 B1, priority to 2/9/1998, cited on PTO-892 mailed 6/30/2004).

The claims are interpreted as drawn to isolated nucleic acids encoding a polypeptide having at least 80% identity to the polypeptide of SEQ ID NO:387, optionally lacking its associated signal peptide, the polypeptide encoded by the full-length coding sequence of SEQ ID NO:386 and encoded by the cDNA deposited under ATCC accession number 203132, wherein the polypeptide optionally induces

chondrocyte redifferentiation (i.e., claims 139-142). Further, the claims are drawn to a vector comprising the nucleic acid encoding said polypeptides, wherein the nucleic acid is operably linked to control sequences and host cells comprising said vector.

Edwards [a] teaches a polynucleotide that encodes a polypeptide (SEQ ID NO:27; columns 125-127) that is 97% identical to the polypeptide of SEQ ID NO:387 (differing only at the C-terminal 6 amino acids), optionally lacking its associated signal peptide (residues 1-14 of SEQ ID NO:387) and therefore, 97% identity with the polypeptide encoded by the full-length coding sequence of SEQ ID NO:386 and encoded by the cDNA deposited under ATCC accession number 203132 (see the alignment attached to the back of this Office Action; Exhibit B). It is noted that amino acid residues 156-157, and 170-171 of SEQ ID NO:27 of Edwards contains codons that would encode arginine residues at amino acids 156-157 and aspartic acid at amino acid 170 and lysine at amino acid 171 and thus, anticipate the sequence of SEQ ID NO:387 at those corresponding amino acid positions.

One of ordinary skill in the art would reasonably conclude that Edwards [a] polypeptide also possesses the same functional properties as those of the polypeptides claimed and, therefore, it appears that Edwards [a] has produced a polynucleotide encoding a polypeptide having the same functional properties as the claimed polypeptides (i.e., induces chondrocyte redifferentiation). Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed polypeptides with the polypeptide of Edwards [a], the burden of proof is upon the Applicant's to show a distinction between the structural and functional characteristics of

the claimed polypeptides and the polypeptide of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Edwards et al [a] also teach vectors comprising said polynucleotide sequence operably linked to control sequences and host cells, including yeast cells (see entire document, particularly columns 83-84). Thus, Edwards et al [a] anticipate the claims.

24. Claims 135-142 are rejected under 35 U.S.C. 102(e) as being anticipated by Edwards et al [b] (U.S. Patent 6,222,029 B1, filed 8/1/1997).

The claims and their interpretation have been described supra.

Edwards [b] teaches a polynucleotide that encodes a polypeptide (SEQ ID NO:27; columns 95-98) that is 97% identical to the polypeptide of SEQ ID NO:387 (differing only at the C-terminal 6 amino acids), optionally lacking its associated signal peptide (residues 1-14 of SEQ ID NO:387) and therefore, 97% identity with the polypeptide encoded by the full-length coding sequence of SEQ ID NO:386 and encoded by the cDNA deposited under ATCC accession number 203132 (see the alignment attached to the back of this Office Action; Exhibit A). It is noted that amino acid residues 156-157, and 170-171 of SEQ ID NO:27 of Edwards [b] contains codons that would encode arginine residues at amino acids 156-157 and aspartic acid at amino acid 170 and lysine at amino acid 171 and thus, anticipate the sequence of SEQ ID NO:387 at those corresponding amino acid positions.

One of ordinary skill in the art would reasonably conclude that Edwards [b] polypeptide also possesses the same functional properties as those of the polypeptides claimed and, therefore, it appears that Edwards [b] has produced a polynucleotide encoding a polypeptide having the same functional properties as the claimed polypeptides (i.e., induces chondrocyte redifferentiation). Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed polypeptides with the polypeptide of Edwards [b], the burden of proof is upon the Applicant's to show a distinction between the structural and functional characteristics of the claimed polypeptides and the polypeptide of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Edwards et al [b] also teach vectors comprising said polynucleotide sequence operably linked to control sequences and host cells, including yeast cells (see entire document, particularly columns 33-34). Thus, Edwards et al [b] anticipate the claims.

Conclusions

25. Claims 124-127 and 129-131 are allowable. The prior art does not teach or fairly suggest a nucleic acid sequence encoding the polypeptide of SEQ ID NO:387 as recited in these claims.

26. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

RESULT 1
US-08-905-223-27
; Sequence 27, Application US/08905223
; Patent No. 6222029
; GENERAL INFORMATION:
; APPLICANT: Edwards, Jean-Baptiste D.
; APPLICANT: Duelert, Aymeric
; APPLICANT: Lacroix, Bruno
; TITLE OF INVENTION: 5' ESTs FOR SECRETED PROTEINS
; NUMBER OF SEQUENCES: 503
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Knobbe, Martens, Olson & Bear
; STREET: 501 West Broadway
; CITY: San Diego
; STATE: California
; COUNTRY: USA
; ZIP: 92101-3505
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy Disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: Win95
; SOFTWARE: Word
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/905,223
; FILING DATE:
; CLASSIFICATION: 536
; ATTORNEY/AGENT INFORMATION:
; NAME: Israelsen, Ned A.
; REGISTRATION NUMBER: 29,655
; REFERENCE/DOCKET NUMBER:
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (619) 235-8550
; TELEFAX: (619) 235-0176
; INFORMATION FOR SEQ ID NO: 27:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 848 base pairs
; TYPE: NUCLEIC ACID
; STRANDEDNESS: DOUBLE
; TOPOLOGY: LINEAR
; MOLECULE TYPE: CDNA
; ORIGINAL SOURCE:

Exhibit A

Exhibit A (continued)

```
;       ORGANISM:  Homo Sapiens
;       DEVELOPMENTAL STAGE:  Fetal
;       TISSUE TYPE:  kidney
;     FEATURE:
;       NAME/KEY:  sig_peptide
;       LOCATION:  32..73
;       IDENTIFICATION METHOD:  Von Heijne matrix
;       OTHER INFORMATION:  score 10.7
;       OTHER INFORMATION:  seq LWLLFFLVTAIHA/EL
US-08-905-223-27

Alignment Scores:
Pred. No.:                3.7e-131      Length:          848
Score:                    1064.00       Matches:         208
Percent Similarity:       97.65%        Conservative:    0
Best Local Similarity:    97.65%        Mismatches:      4
Query Match:              96.55%        Indels:          1
DB:                       3             Gaps:            0

US-09-989-724-387 (1-212) x US-08-905-223-27 (1-848)

Qy          1 MetLeuTrpLeuLeuPhePheLeuValThrAlaIleHisAlaGluLeuCysGlnProGly 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         32 ATGTTGTGGCTGCTCTTTTTTCTGGTGACTGCCATTCATGCTGAACTCTGTCAACCAGGT 91

Qy         21 AlaGluAsnAlaPheLysValArgLeuSerIleArgThrAlaLeuGlyAspLysAlaTyr 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         92 GCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCATAT 151

Qy         41 AlaTrpAspThrAsnGluGluTyrLeuPheLysAlaMetValAlaPheSerMetArgLys 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        152 GCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA 211

Qy         61 ValProAsnArgGluAlaThrGluIleSerHisValLeuLeuCysAsnValThrGlnArg 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        212 GTTCCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGG 271

Qy         81 ValSerPheTrpPheValValThrAspProSerLysAsnHisThrLeuProAlaValGlu 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        272 GTATCATTCTGGTTTGTGGTTACAGACCCTTCAAAAAATCACACCCTTCCTGCTGTTGAG 331

Qy        101 ValGlnSerAlaIleArgMetAsnLysAsnArgIleAsnAsnAlaPhePheLeuAsnAsp 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        332 GTGCAATCAGCCATAAGAATGAACAAGAACCGGATCAACAATGCCTTCTTTCTAAATGAC 391

Qy        121 GlnThrLeuGluPheLeuLysIleProSerThrLeuAlaProProMetAspProSerVal 140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        392 CAAACTCTGGAATTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTG 451

Qy        141 ProIleTrpIleIleIlePheGlyValIlePheCysIleIleIleValAlaIleAlaLeu 160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        452 CCCATCTGGATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCACTA 511

Qy        161 LeuIleLeuSerGlyIleTrpGlnArgArgArgLysAsnLysGluProSerGluValAsp 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        512 CTGATTTTATCAGGGATCTGGCAACGTADAARAAAGAACAAAGAACCATCTGAAGTGGAT 571

Qy        181 AspAlaGluAspLysCysGluAsnMetIleThrIleGluAsnGlyIleProSerAspPro 200
              |||||||||  ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        572 GACGCTGAARATAAKTGTGAAAACATGATCACAATTGAAAATGGCATCCCCTCTGATCCC 631

Qy        201 LeuAspMetLysGly-GlyIleLeuMetMetProSer 212
              |||||||||||||| ||||||||||||||||||||||
Db        632 CTGGACATGAAGGGAGGGCATATTAATGATGCCTTCA 668

RESULT 2
US-09-247-155-27
; Sequence 27, Application US/09247155A
; Patent No. 6312922
; GENERAL INFORMATION:
;  APPLICANT: Dumas Milne Edwards, Jean-Baptiste
;  APPLICANT: Duclert, Aymeric
;  APPLICANT: Bougueleret, Lydie
;  TITLE OF INVENTION: Complementary DNAs
;  FILE REFERENCE: GENSET.021A
;  CURRENT APPLICATION NUMBER: US/09/247,155A
;  CURRENT FILING DATE: 1999-02-09
;  EARLIER APPLICATION NUMBER: 60/074,121
;  EARLIER FILING DATE: 1998-02-09
;  EARLIER APPLICATION NUMBER: 60/081,563
;  EARLIER FILING DATE: 1998-04-13
;  EARLIER APPLICATION NUMBER: 60/096,116
;  EARLIER FILING DATE: 1998-08-10
;  EARLIER APPLICATION NUMBER: 60/099,273
;  EARLIER FILING DATE: 1998-10-04
;  NUMBER OF SEQ ID NOS: 182
;  SOFTWARE: Patent.pm
; SEQ ID NO 27
;   LENGTH: 848
;   TYPE: DNA
;   ORGANISM: Homo Sapiens
;   FEATURE:
;   NAME/KEY: sig_peptide
;   LOCATION: 32..73
;   OTHER INFORMATION: Von Heijne matrix
US-09-247-155-27
```

Exhibit B

```
Alignment Scores:
Pred. No.:                3.7e-131      Length:          848
Score:                    1064.00       Matches:         208
Percent Similarity:       97.65%        Conservative:    0
Best Local Similarity:    97.65%        Mismatches:      4
Query Match:              96.55%        Indels:          1
DB:                       3             Gaps:            0

US-09-989-724-387 (1-212) x US-09-247-155-27 (1-848)

Qy          1 MetLeuTrpLeuLeuPhePheLeuValThrAlaIleHisAlaGluLeuCysGlnProGly 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         32 ATGTTGTGGCTGCTCTTTTTTCTGGTGACTGCCATTCATGCTGAACTCTGTCAACCAGGT 91

Qy         21 AlaGluAsnAlaPheLysValArgLeuSerIleArgThrAlaLeuGlyAspLysAlaTyr 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         92 GCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCATAT 151

Qy         41 AlaTrpAspThrAsnGluGluTyrLeuPheLysAlaMetValAlaPheSerMetArgLys 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        152 GCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA 211

Qy         61 ValProAsnArgGluAlaThrGluIleSerHisValLeuLeuCysAsnValThrGlnArg 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        212 GTTCCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGG 271

Qy         81 ValSerPheTrpPheValValThrAspProSerLysAsnHisThrLeuProAlaValGlu 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        272 GTATCATTCTGGTTTGTGGTTACAGACCCTTCAAAAAATCACACCCTTCCTGCTGTTGAG 331

Qy        101 ValGlnSerAlaIleArgMetAsnLysAsnArgIleAsnAsnAlaPhePheLeuAsnAsp 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        332 GTGCAATCAGCCATAAGAATGAACAAGAACCGGATCAACAATGCCTTCTTTCTAAATGAC 391

Qy        121 GlnThrLeuGluPheLeuLysIleProSerThrLeuAlaProProMetAspProSerVal 140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        392 CAAACTCTGGAATTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTG 451

Qy        141 ProIleTrpIleIleIlePheGlyValIlePheCysIleIleIleValAlaIleAlaLeu 160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        452 CCCATCTGGATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCACTA 511

Qy        161 LeuIleLeuSerGlyIleTrpGlnArgArgArgLysAsnLysGluProSerGluValAsp 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        512 CTGATTTTATCAGGGATCTGGCAACGTADAARAAAGAACAAAGAACCATCTGAAGTGGAT 571

Qy        181 AspAlaGluAspLysCysGluAsnMetIleThrIleGluAsnGlyIleProSerAspPro 200
              |||||||||  ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        572 GACGCTGAARATAAKTGTGAAAACATGATCACAATTGAAAATGGCATCCCCTCTGATCCC 631

Qy        201 LeuAspMetLysGly-GlyIleLeuMetMetProSer 212
              |||||||||||||| ||||||||||||||||||||||
Db        632 CTGGACATGAAGGGAGGGCATATTAATGATGCCTTCA 668
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